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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,012	04/01/2005	Frank Watjen	2815-0304PUS1	7865

2292 7590 03/19/2008
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EXAMINER	
CHANG, CELIA C	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
03/19/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/530,012	WATJEN, FRANK	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of group I in the reply filed on Jan. 7, 2008 is acknowledged. The traversal is on the grounds that the method claims should be rejoined. The method claims 10-12 are rejoined. Claims 1-12 are pending.

2. Claims 9-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916), where the Supreme Court looked to whether the experimentation needed to practice an invention was undue or unreasonable. *Id.* An invention must be described so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988). As stated in the MPEP 2164.01(a) "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". The analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole. *Id.* at 740, *Id.* at 1407. The factors to be considered herein are those set forth as the In re Wands, 8 USPQ 2nd 1400 (1988) decision.

The analysis is applied to the instant case.

Nature of invention

The claims are drawn to making and using composition containing compounds of claims 1-8 for the treatment of disease or disorder or a condition of a living animal body including a human which disorder, disease or condition is responsive to inhibition of monoamine neurotransmitter reuptake.

The scope is considered a reach through process since it is intended to include any and all condition which involves monoamine neurotransmission not yet discovered at the time the invention was made.

The state of the art and predictability

The specification provided no testing of the compounds but relied upon WO97/30997 (1449) testing protocol for the instant utility and treatment of diseases or disorders. The instantly claimed compounds draw no structural similarity or analogue to the prior art compounds disclosed by Kruger et al. '997. The Kruger compounds are bridged ring compounds. In addition, Kruger et al. '997 compounds are in vitro inhibitors for all dopamine, noradrenaline and 5HT reuptake. Therefore, no support for the instant compounds which is structurally diverse from the '997 and having only dopamine reuptake inhibition.

Structurally similar compounds as demonstrated by the previous office action such as US 6,440,996 are useful as intermediates thus non-pharmacological use, or having gastrointestinal motility use (see EP 190,496).

The amount of guidance and working examples

The specification provided no data on the binding activity of the instantly claimed compound. It was clearly disclosed in the specification reflecting the state of understanding of the neurotransmitter reuptake intervention art that is the "activity on reuptake of the monoamine neurotransmitters, serotonin, dopamine and noradrenaline, such as the ration of the serotonin reuptake versus the noradrenaline and dopamine activity" (p.2). For therapeutic and/or pharmacological activity of a given compound, non-specific binding or activity provided no utility. Only when the particularity in selective binding will the compounds be useful in therapy. Such teaching of the prior art is not only disclosed on page 2, but also well recognized by artisan in the field (see Kung et al.). The specification provided no information as to the binding activity, or the relationship among the binding of the interacting neurotransmitters as to provide sufficient guidelines for one having ordinary skill to construct dosage in composition for the relevant activity (see Akunne or CA 115). Absent of testing data, relational activity among the interacting neutotransmitters, and specific binding correlated to the utility, the specification provided insufficient guidelines for one skilled in the art to construct pharmaceutical compositions or to operate treatment from mood disorder....neuropathic pain.....tourettes disease. Applicants provided no nexus that currently, there is any one compound will have efficacy in all the disorders as listed in claim 12, let alone a group of compounds with structure diversity.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Christensen et al. US 3912743 supplemented with CA 81 in view of Ciganek US 4,485,109 or Kozikowski et al. US 6,180,648 further in view of Kuroita et al. CA132.

Determination of the scope and content of the prior art (MPEP §2141.01)

Christensen et al. '743 disclosed 4-substituted phenyl piperidinyl compounds which are made from the intermediates having the CH2-ORc moiety at the 3-position of the piperidinyl ring (see CA 81 structural delineation). Such intermediates are for making the products having CNS activity and the examples have a single substitution on the 4-phenyl moiety. Ciganek '109, or Kozikowski et al. '846 taught that the 4-phenyl substitutents can be optionally multiple substituted (see '109 col. 22, line33-40, '648, col. 22, lines 21-25).

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The instant claims are drawn to compounds wherein Ra and Rb are at the 3,4-positions and are halogens and the difference between the instant claims from the prior art is that the dihalo substitution at the 3,4 position was not exemplified. The 4-(3,4-dichlorophenyl) piperidinyl moiety being a core structure of CNS active compounds have been well recgnized in the art (see CA 132).

Finding of prima facie obviousness---rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art in possession of the above references is in possession of the instant claims **because** the prior art provided the technical skill, the generic teaching and motivation for one to pick the 3,4-dihalo substituted intermediates since such picking and choosing have been taught by analogous art and demonstrated to be useful in making CNS active compounds. In absent of unexpected results, there is nothing unobvious in picking some i.e the specific 3,4-dihalo, among the many optional choices ('109, col.5-6, table 1, compound 13) well documented in the art.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang, Ph. D. whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Mar. 10, 2009

/Celia Chang/
Primary Examiner
Art Unit 1625